```
=> d his

     (FILE 'HOME' ENTERED AT 12:02:18 ON 28 SEP 2010)

     FILE 'CAPLUS' ENTERED AT 12:02:43 ON 28 SEP 2010
                E YIM PS/AU
L1          2199 S URINARY (2A) INCONTINENCE
L2         50810 S OPIOID
L3            31 S L1 (L) L2
L4             1 S L3 AND PY=1996
L5            45 S L1 AND L2
L6             1 S L5 AND 1996/PY

=> s detrusor
           2020 DETRUSOR
             32 DETRUSORS
L7         2021 DETRUSOR
                (DETRUSOR OR DETRUSORS)

=> s l2 and l7
L8           28 L2 AND L7

=> s l2 (L) l7
L9           24 L2 (L) L7


=> d ti 1-24 l9
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y



L9   ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   Exogenously administered opioids contract the female rat intrinsic
     urethral sphincter in vivo

L9   ANSWER 2 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   The Effects of Spinal Anesthesia with Lidocaine and Sufentanil on Lower
     Urinary Tract Functions

L9   ANSWER 3 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   Emerging drugs for treatment of overactive bladder and detrusor
     overactivity

L9   ANSWER 4 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   Drug-induced urinary retention: incidence, management and prevention

L9   ANSWER 5 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   Effect of lumber-epidural administration of tramadol on lower urinary
     tract function

L9   ANSWER 6 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   Muscarinic receptor antagonists for overactive bladder

L9   ANSWER 7 OF 24  CAPLUS  COPYRIGHT 2010 ACS on STN
TI   Reversal of opioid-induced bladder dysfunction by intravenous naloxone and
     methylnaltrexone
```

L9 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction

L9 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Treatment-resistant detrusor overactivity - underlying pharmacology and potential mechanisms

L9 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Daily intravesical instillation of 1 mg nociceptin/orphanin FQ for the control of neurogenic detrusor overactivity: a multicenter, placebo controlled, randomized exploratory study

L9 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI DPI-221 [4-((α-S)-α-((2S,5R)-2,5-dimethyl-4-(3-fluorobenzyl)-1-piperazinyl) benzyl)-N,N-diethylbenzamide]: A novel nonpeptide δ receptor agonist producing increased micturition interval in normal rats

L9 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Differential roles of peripheral and spinal endothelin receptors in the micturition reflex in rats

L9 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Intrathecal Opioids and Lower Urinary Tract Function: A Urodynamic Evaluation

L9 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Potential therapeutic targets for the treatment of detrusor overactivity

L9 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Roles of Opiate in Lower Urinary Tract Dysfunction Associated with Spinal Cord Injury in Rats

L9 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI CNS involvement in overactive bladder: pathophysiology and opportunities for pharmacological intervention

L9 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Tramadol Inhibits Rat Detrusor Overactivity Caused by Dopamine Receptor Stimulation

L9 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Pharmacological agents for the treatment of urinary incontinence due to overactive bladder

L9 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI The urodynamic effects of intravenous opioids and ketoprofen in humans

L9 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Anticholinergic and calcium antagonistic activities of NS-21 contribute to the inhibition of rat urinary bladder contractions

L9 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Possible regulatory role of dynorphin A in the urinary bladder

L9 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Involvement of **opioid** mechanisms in peripheral motor control of **detrusor** muscle

L9 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI In vivo motor effects of loperamide on the rat urinary bladder

L9 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
TI Central and peripheral motor effects of morphine on the rat urinary bladder

=> d l9 ibib abs hitind 3 4 6 8 9 14 17 18 22
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

L9 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:1057353 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 150:297352
TITLE: Emerging drugs for treatment of overactive bladder and detrusor overactivity
AUTHOR(S): Drake, Marcus J.
CORPORATE SOURCE: Bristol Urological Institute, Southmead Hospital, Bristol, BS10 5NB, UK
SOURCE: Expert Opinion on Emerging Drugs (2008), 13(3), 431-446
CODEN: EOEDA3; ISSN: 1472-8214
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Overactive bladder (OAB) signifies the presence of urinary urgency and can have major effects on quality of life and social functioning. Standard antimuscarinic drugs have good initial response rates but substantial adverse effects and long-term compliance problems. To review the complexities of the mechanisms underlying OAB and the current drugs available for treating its symptoms. The literature was reviewed to define current therapies and drugs in clin. trials. Articles were identified by means of a computerized PubMed and Cochrane Library search (using the following keywords: overactive bladder, detrusor overactivity, urgency and bladder), supported by a search of the PharmaProjects database. New drug classes, such as beta-3 adrenergic agonists, may work by reducing contractility or excitability of bladder muscle. Moderation of afferent activity may allow improved OAB symptoms, with lower risk of affecting voiding function. Agents acting on the CNS could influence OAB favorably, but target selection and adverse effects are an issue. The recognition of the functional contribution of the urothelium and the diversity of nerve transmitters has sparked interest in both peripheral and central modulation of OAB pathophysiol.
CC 1-0 (Pharmacology)
IT **Opioid** receptor antagonists
(μ- **opioid**; emerging drugs for treatment of overactive bladder and **detrusor** overactivity)
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 178 THERE ARE 178 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:701356 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 149:118409

TITLE: Drug-induced urinary retention: incidence, management and prevention
AUTHOR(S): Verhamme, Katia M. C.; Sturkenboom, Miriam C. J. M.; Stricker, Bruno H. Ch; Bosch, Ruud
CORPORATE SOURCE: Pharmacoepidemiology Unit, Department of Medical Informatics and Epidemiology and Biostatistics, Erasmus University Medical Centre, Rotterdam, Neth.
SOURCE: Drug Safety (2008), 31(5), 373-388
CODEN: DRSAEA; ISSN: 0114-5916
PUBLISHER: Wolters Kluwer Health
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Urinary retention is a condition in which impaired emptying of the bladder results in postvoidal residual urine. It is generally classified into "acute" or "chronic" urinary retention. Because of the complex mechanism of micturition, many drugs can interact with the micturition pathway, all via different modes of action. Although the incidence of urinary retention, in particular acute urinary retention, has been well studied in observational studies and randomized controlled trials, data on the incidence of drug-induced urinary retention are scarce. Data from observational studies suggest that up to 10% of episodes might be attributable to the use of concomitant medication. Urinary retention has been described with the use of drugs with anticholinergic activity (e.g. antipsychotic drugs, antidepressant agents and anticholinergic respiratory agents), **opioids** and anesthetics, α-adrenoceptor agonists, benzodiazepines, NSAIDs, **detrusor** relaxants and calcium channel antagonists. Elderly patients are at higher risk for developing drug-induced urinary retention, because of existing co-morbidities such as benign prostatic hyperplasia and the use of other concomitant medication that could reinforce the impairing effect on micturition. Drug-induced urinary retention is generally treated by urinary catheterization, especially if acute, in combination with discontinuation or a reduction in dose of the causal drug. Studies have been carried out examining the effects of preventive measures for anesthesia-related urinary retention, both during and after surgery, particularly into the effect of using **opioids** in combination with non-**opioid** analgesic drugs on the incidence of postoperative urinary retention. Although combination therapy reduces the **opioid**-related adverse events, the effect on urinary retention yields contradictory results. This article reviews the literature on drug-induced urinary retention and focuses on its incidence, the different classes of drugs that have been associated with it, and options for its management and prevention.

CC 1-0 (Pharmacology)
IT Analgesics
Drug toxicity
Drug withdrawal
Dysuria
Human
(anticholinergic, antipsychotic, antidepressant, **opioid**, anesthetic, α-adrenoceptor agonist, benzodiazepine, NSAID, **detrusor** relaxant and calcium channel antagonist may be associated with urinary retention in elderly patient)
IT Aging, animal
(elderly; anticholinergic, antipsychotic, antidepressant, **opioid**, anesthetic, α-adrenoceptor agonist, benzodiazepine, NSAID, **detrusor** relaxant and calcium channel antagonist may be associated with urinary retention in elderly patient)
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD

(2 CITINGS)
REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:1353800 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 148:182204
TITLE: Muscarinic receptor antagonists for overactive bladder
AUTHOR(S): Abrams, Paul; Andersson, Karl-Erik
CORPORATE SOURCE: Bristol Urological Institute, Southmead Hospital, Bristol, UK
SOURCE: BJU International (2007), 100(5), 987-1006
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Overactive bladder (OAB) is a syndrome characterized by urinary urgency, with or without urgency urinary incontinence, usually with frequency and nocturia. OAB symptoms are often associated with **detrusor** overactivity (DO). Like OAB symptoms, the prevalence of DO increases with age and can have a neurogenic and/or myogenic etiol. Bladder outlet obstruction can be a contributing factor in DO, possibly through cholinergic denervation of the **detrusor** and supersensitivity of muscarinic receptors to acetylcholine, although the prevalence of OAB is similar in men and women across age groups. Acetylcholine is the primary contractile neurotransmitter in the human **detrusor**, and antimuscarinics exert their effects on OAB/DO by inhibiting the binding of acetylcholine at muscarinic receptors M2 and M3 on **detrusor** smooth muscle cells and other structures within the bladder wall. Worldwide, there are six antimuscarinic drugs currently marketed for the treatment of OAB: oxybutynin, tolterodine, propiverine, trospium, darifenacin, and solifenacin. Each has demonstrated efficacy for the treatment of OAB symptoms, but their pharmacokinetic and adverse event profiles differ somewhat due to structural differences (tertiary vs quaternary amines), muscarinic receptor subtype selectivities, and organ selectivities. Antimuscarinics are generally well tolerated, even in special populations (e.g. men with bladder outlet obstruction, elderly patients, children). The most frequently reported adverse events in clin. studies of antimuscarinics are dry mouth, constipation, headache, and blurred vision; few patients withdraw from clin. trials because of adverse events. Development of an antimuscarinic with functional selectivity for the bladder would reduce the occurrence of antimuscarinic adverse events. The therapeutic potential of several other agents, such as α3-adrenoceptor agonists, purinergic receptor antagonists, phosphodiesterase inhibitors, neurokinin-1 receptor antagonists, **opioids**, and Rho-kinase inhibitors, is also under investigation for the treatment of OAB.
CC 1-0 (Pharmacology)
OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 212 THERE ARE 212 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:501533 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 147:314837
TITLE: Effects of **opioid** subtypes on

detrusor overactivity in rats with cerebral infarction

AUTHOR(S): Nagasaka, Yasuhiro; Yokoyama, Osamu; Komatsu, Kazuto; Ishiura, Yoshiyuki; Nakamura, Yasuo; Namiki, Mikio

CORPORATE SOURCE: Department of Urology, School of Medicine, Kanazawa University, Kanazawa, Japan

SOURCE: International Journal of Urology (2007), 14(3), 226-231
CODEN: IJURF3; ISSN: 0919-8172

PUBLISHER: Blackwell Publishing Asia Pty Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Aim: In order to determine the influence of different **opioid** receptor subtypes on **detrusor** overactivity after left middle cerebral artery (MCA) occlusion, cystometric recordings were obtained in conscious rats. Methods: Female Sprague-Dawley rats were used in this study. Control cystometrog. was followed by left MCA occlusion. The sham-operated (SO) rats underwent the same procedures except for MCA occlusion. [D-Ala2,Phe4,Gly5]-enkephalin (DAGO; μ- **opioid** agonist), [D-Pen2.5]-enkephalin (DPDPE; δ1- **opioid** agonist), deltorphin II (δ2- **opioid** agonist), and U-50488 (κ- **opioid** agonist) were administered intracerebroventricularly at graded doses. The bladder capacity, residual volume, micturition threshold pressure, and bladder contraction pressure were determined Finally, the volume of the infarction was measured. Results: The intracerebroventricular administration of DAGO and DPDPE significantly increased the bladder capacity in the cerebrally infarcted (CI) and 50 rats, but differences in the changes in bladder capacity between the CI and SO rats were not significant. Deltorphin II did not produce any changes in the bladder capacity in the CI or SO rats at any dose examined However, the intracerebroventricular administration of U-50488 significantly increased the bladder capacity in the CI rats but not in the SO rats. None of the drugs affected the residual volume, micturition threshold pressure or bladder contraction pressure at any dosage examined The mean infarcted vols. were not significantly different from those in the vehicle-treated rats. Conclusion: These results suggest that the **opioid** receptor subtypes, μ and δ1 in the brain, are related to the micturition reflex. Furthermore, the κ **opioid** agonist might be useful for the suppression of **detrusor** overactivity caused by cerebral infarction.

CC 1-11 (Pharmacology)

ST cerebral infarction **detrusor** overactivity **opioid** receptor

IT Bladder
(**detrusor** muscle; effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)

IT Brain infarction
(effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)

IT κ- **Opioid** receptors
μ- **Opioid** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)

IT **Opioids**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)

IT Reflex

(micturition; effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)
IT δ- **Opioid** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(δ1; effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)
IT δ- **Opioid** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(δ2; effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)
IT 78123-71-4, DAGO 88373-73-3
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of **opioid** subtypes on **detrusor** overactivity in rats with cerebral infarction)
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:104368 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 146:243053
TITLE: Treatment-resistant detrusor overactivity - underlying pharmacology and potential mechanisms
AUTHOR(S): Andersson, K.-E.
CORPORATE SOURCE: Department of Clinical and Experimental Pharmacology, Lund University Hospital, Lund, Swed.
SOURCE: International Journal of Clinical Practice, Supplement (2006), 151, 8-16
CODEN: ICPSFY; ISSN: 1368-504X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Bladder function during filling and micturition is regulated by peripheral and central nervous and hormonal control systems. Micturition occurs in response to afferent signals from the lower urinary tract, and distention of the bladder wall is the primary stimulus. In the animal and human bladder, efferent adrenergic, cholinergic and nonadrenergic, noncholinergic (NANC) neurotransmission has been demonstrated. The most important receptors for activation of contraction are muscarinic (M3) and purinergic receptors (P2X1), however, the contribution of these receptors to contraction may differ between species, and may be changed in bladder dysfunction associated with **detrusor** overactivity (DO) and/or the overactive bladder (OAB) syndrome, such as outflow obstruction, neurogenic bladders, idiopathic DO and diabetes. The NANC component of the nerve-induced response in such disorders may be responsible for up to 40-50% of the total bladder contraction. Whether this in vitro 'atropine-resistance' corresponds to DO/OAB seen in patients not responding to antimuscarinic treatment is not known. Afferent signalling from the urothelium may be involved in both normal bladder function and in DO/OAB, but its role in antimuscarinic-refractory patients remains to be established. Several central nervous system (CNS) transmitters/transmitter systems, including gamma aminobutyric acid (GABA), **opioid**, serotonin, noradrenaline, dopamine or glutamatergic receptors and mechanisms are known to be involved in micturition control. The contribution of these receptors and mechanisms in DO/OAB resistant to treatment with antimuscarinics is not known, but drugs acting at these sites may offer future treatment possibilities.
CC 1-0 (Pharmacology)

IT **Opioids**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(central nervous system transmitters/transmitter systems including **opioid** are involved in micturition control in patient with **detrusor** overactivity)
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2004:267997 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 141:324932
TITLE: Potential therapeutic targets for the treatment of detrusor overactivity
AUTHOR(S): Chess-Williams, Russell
CORPORATE SOURCE: Department of Biomedical Science, University of Sheffield, Sheffield, S10 2TN, UK
SOURCE: Expert Opinion on Therapeutic Targets (2004), 8(2), 95-106
CODEN: EOTTAO; ISSN: 1472-8222
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Current treatments for the overactive **detrusor** are poorly tolerated and can exert significant adverse effects. Possible targets for the development of new treatments are considered. Potential targets in four locations are examined: **detrusor** smooth muscle, urothelium, peripheral nerves and the CNS. In the **detrusor**, the role of various muscarinic receptor subtypes is discussed and β-adrenoceptor agonists, phosphodiesterase inhibitors and potassium channel openers, all of which inhibit **detrusor** contractility, are considered for drug development. In the urothelium, a number of substances are released that affect bladder function including ATP, acetylcholine and an inhibitory factor that has yet to be identified. All three systems have the potential to be novel targets for drug development. Other possible therapeutic targets are the mechanisms influencing transmitter release in the bladder, for example, prejunctional 5-hydroxytryptamine (5-HT)4 receptors. Finally, targets within the CNS and spinal cord are considered, including **opioid** receptors, 5-HT receptors and α-adrenoceptors.
CC 1-0 (Pharmacology)
OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 142 THERE ARE 142 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:468911 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 140:35735
TITLE: Tramadol Inhibits Rat Detrusor Overactivity Caused by Dopamine Receptor Stimulation
AUTHOR(S): Pehrson, Rikard; Andersson, Karl-Erik
CORPORATE SOURCE: Department of Clinical Pharmacology, Lund University Hospital, Lund, S-221 85, Swed.
SOURCE: Journal of Urology (Hagerstown, MD, United States) (2003), 170(1), 272-275
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal
LANGUAGE: English
AB PURPOSE: In patients with Parkinson's disease an imbalance between stimulatory D2-like receptors and inhibitory D1-like receptors may contribute to **detrusor** overactivity. Apomorphine, which stimulates D1-like and D2-like dopamine receptors, induces **detrusor** overactivity in rats. Tramadol is an analgesic drug that stimulates **opioid** receptors and inhibits reuptake of serotonin and noradrenaline. To evaluate a potentially inhibitory effect of tramadol the drug was given to rats with apomorphine induced **detrusor** overactivity. MATERIAL AND METHODS: Female Sprague-Dawley rats were used. During anesthesia catheters were introduced into the bladder dome, femoral vein and s.c. Three days later the rats were placed in a metabolism cage and voiding was stimulated by infusing saline into the bladder. Micturition parameters were recorded and compared after the administration of apomorphine and tramadol or vehicle. Desmopressin was given as pretreatment to suppress the diuresis produced by tramadol. RESULTS: While 30 μg kg-1 apomorphine s.c. was devoid of effect, 60 and 100 μg kg-1 apomorphine s.c. induced a transient **detrusor** overactivity. Tramadol (1 mg kg-1) was without effect but 5 and 10 mg kg-1 tramadol i.v. attenuated the effects of apomorphine, while inducing prominent diuresis. Pretreatment with desmopressin, which did not alter cystometry or the effects of apomorphine, abolished diuresis. In these rats 5 and 10 mg kg-1 tramadol i.v. abolished the overactivity caused by apomorphine s.c. CONCLUSIONS: Tramadol effectively suppresses apomorphine induced **detrusor** overactivity in doses shown to have analgesic activity. Hence, tramadol may provide an approach to treat lower urinary tract disorders in which dopamine receptor activation is involved.
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:9932 CAPLUS <<LOGINID::20100928>>
DOCUMENT NUMBER: 134:141266
TITLE: Pharmacological agents for the treatment of urinary incontinence due to overactive bladder
AUTHOR(S): Wein, Alan J.
CORPORATE SOURCE: Division of Urology, University of Pennsylvania Health System, Philadelphia, PA, 19104, USA
SOURCE: Expert Opinion on Investigational Drugs (2001), 10(1), 65-83
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 69 refs. Although the exact etiol. of overactive bladder is unknown to date, pharmacol. therapy has been targeted to both the central and peripheral nervous systems. Potential CNS targets include GABA, **opioid**, serotonin (5-HT), dopamine and glutaminergic receptors as well as the α-adrenoceptors. Potential PNS targets include muscarinic receptors, calcium and potassium channels and α- and β-adrenergic receptors. Since acetylcholine is the primary excitatory neurotransmitter involved in bladder (**detrusor**) contraction and emptying, anticholinergic agents are the primary compds.

used clin. to decrease involuntary **detrusor** contractions. Anticholinergic therapy has a stabilizing effect on the bladder (**detrusor** muscle); increases bladder capacity; decreases frequency of involuntary **detrusor** contractions; and delays the initial urge to void, but does not affect warning time. However, the clin. utility of antimuscarinic therapy is limited by the lack of receptor selectivity, resulting in the classic anticholinergic side effects of dry mouth, blurred vision, constipation and potentially, CNS effects such as somnolence and impaired cognitive function. These unwanted side effects often result in premature discontinuation of therapy and poor compliance. Previous attempts to develop uroselective α-adrenergic receptor antagonists have not been successful and although research continues, the hope that this class of agents would be viable alternatives to the anticholinergics remains to be proven in the clin. setting. The recent demise of several potassium channel openers does not augur well for the future of this class of agent. The reasons for the discontinuation of trials with these agents have not been fully elucidated, but one must assume that they were not uroselective and the cardiovascular side effects rendered them less than useful clin. The serotonin re-uptake inhibitors appear to be promising novel therapeutic agents aimed at controlling bladder over-activity through specific CNS pathways. The sensory side of the micturition reflex is a potential therapeutic target. Agents to desensitize afferent nerve endings involved in C-fiber afferent reflexes include capsaicin and resiniferatoxin. Their clin. applicability is currently being evaluated. Finally, the recent findings related to the role of the P2X3 receptor in the sensory aspects of bladder filling have created new interest in the future development of agents that will improve the management of this prevalent and debilitating condition.

CC 1-0 (Pharmacology)

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1992:626192 CAPLUS <<LOGINID::20100928>>

DOCUMENT NUMBER: 117:226192

ORIGINAL REFERENCE NO.: 117:38869a,38872a

TITLE: Involvement of **opioid** mechanisms in peripheral motor control of **detrusor** muscle

AUTHOR(S): Berggren, A.; Rubenson, A.; Sillen, U.

CORPORATE SOURCE: Dep. Paediatr. Surg., Oestra Sjukhuset, Goeteborg, S-416 85, Swed.

SOURCE: Pharmacology & Toxicology (Oxford, United Kingdom) (1992), 71(3, Pt. 1), 179-84
CODEN: PHTOEH; ISSN: 0901-9928

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Isometric recordings of the mech. activity in muscle strips from the rat and human urinary bladder **detrusor** were performed and the effects of μ- and δ- **opioid** receptor stimulation and blockade on contractions induced by elec. field stimulation were tested. Stimulation of the **opioid** μ-receptor with morphine (10-13 to 10-4 M) and DAGO (10-13 to 10-6 M) had no effect on elec. field stimulation except at one concentration of morphine (10-6 M). Naloxone (10-10 to 10-5 M) facilitated the elec. field stimulation-induced contraction, which was counteracted by morphine (10-8 M) and the δ-agonist DPDPE (10-8 M) in both rat and human **detrusors**. Addition of atropine (10-6 M)

or hexamethonium chloride (10-6 M) or spantide (10-6 M) did not alter the facilitating effect of naloxone in the rat **detrusor**. Hexamethonium (10-5 M) decreased the facilitating effect of naloxone on elec. field stimulation-induced contractions in the human **detrusor**, indicating an involvement of ganglionic mechanisms. In the human **detrusor**, about 15% of the contractile response was atropine-resistant (10-6 M) and one third of this was resistant to tetrodotoxin (1.5 + 10-6 M). The atropine-resistant response in the human **detrusor** was facilitated by naloxone to the same extent as the atropine-sensitive part. Adrenergic blockade by phentolamine mesylate (10-6 M) and propranolol (10-6 M), facilitated the elec. field stimulation-induced contraction in the rat **detrusor** but did not affect the facilitating effect of naloxone (10-13 to 10-5 M). Addition of the δ-agonist DPDPE (10-13 to 10-5 M) did not change the **detrusor** response to elec. field stimulation in the rat **detrusor**, but the δ-antagonist naltrindole (10-13 to 10-5 M) facilitated it at the highest concentration In the human **detrusor**, DPDPE (10-8 M) reduced the response induced by elec. field stimulation. Thus, blockade of the **opioid** receptors with naloxone facilitates the **detrusor** contraction elicited by elec. field stimulation. The existence of a tonic inhibitory action on the **detrusor** nerve-mediated **detrusor** contraction by **opioid** μ- and possibly δ-receptors is suggested.

CC 1-11 (Pharmacology)
Section cross-reference(s): 13

ST bladder **detrusor** contraction **opioid** receptor mechanism

IT Bladder
(**detrusor** muscle, contractions of, **opioid** mechanisms in, in human and rat)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)